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(54) Title: COSMETIC AND PHARMACEUTICAL COMPOSITIONS AND THEIR USE

(57) Abstract: Pharmaceutical and cosmetical compositions comprising a chelating and a sequestering agent, and optionally containing further ingredients. Use of such compositions to make water more compatible with the skin. Use of such compositions to prevent or treat skin conditions such as eczema, irritation and skin dryness.

Cosmetic and Pharmaceutical Compositions and Their Use

This invention is concerned with cosmetic or pharmaceutical compositions comprising a chelating and a sequestering agent and optionally further components. The invention further concerns the preparation of said compositions and their use in the prevention or topical treatment of skin conditions such as eczema, irritation and skin dryness, as well the use of these compositions for making water more compatible with the skin.

Background of the Invention

Water is omnipresent in the biosphere and is an integral and even the most abundant part of the of the human body, including its outer part, more in particular the skin. However, in certain circumstances water can have adverse effects on the human body, in particular on the skin. In fact the "beneficial window"of water is quite small compared to certain other chemicals, having a safety factor of about 4 to 5. The undesired effects of water, especially with regard to the skin, are largely dependent on water quality. The latter in turn depends on certain components that are present in water, in particular on the presence of ionic components. But even pure water is known to dry out healthy skin. Hard water on the other hand may lead to calcium precipitates on the skin that may cause drying, irritation and even atopic eczema. It has been demonstrated that the incidence of atopic eczema in school children is higher in areas with hard water compared with areas with soft water. Another problem associated with the usage of hard water is the decreased performance of cosmetic cleansers.

It is therefore an object of the present invention to prevent these undesired side effects of water to the skin and in particular to prevent the incidence of drying, irritation and atopic eczema. It is a further object to make water more compatible to the skin and to provide new compositions that lack the adverse effects relating to the use of water and in particular the use of hard water.

It is still a further object to provide compositions that prevent the formation of calcium precipitates, thus leading to a healthier skin, while at the same time improving the performance of cosmetic cleansers such as e.g. soaps, shampoos, shower gels and the like.

EP-0884344 and EP-0884380 describe mild surfactant compositions comprising hydrophobic modified polyaspartic acid derivatives for cosmetic and cleansing use. These compositions are taught to be mild, but there is no mentioning of water quality or skin compatiblity of water, only a discription of antimicrobial action is given.

EP-0958811 describes modified polyaspartic acid in oil/water based emulsions for use in cosmetic applications such as day or night creams, moisturizing creams, body lotions and the like.

EP-0959093 describes a pigment paste containing derivatives of polyaspartic acid.

WO-00/49121 describes compositions for washing and cleaning, which compositions contain spray-dried polyaspartic acid and/or iminodisuccinates.

US-5,540,863 describes polyamino acids or their salts mixed with citric acid or its salts used to chelate calcium ions.

EP-0412705 describes a vehicle system for providing a desirable rheology of products formulated therewith, enhanced dispersion of actives therein, and improved deposition of actives therefrom. The vehicle system optionally contains a chelating agent.

WO-99/62482 discloses transparent cosmetic preparations containing a particular surfactant and a sequestering agent.

US-5,635,167 relates to a process for the removal of exogenous minerals which have become attached to hair being based on the usage of particular chelating agents.

WO-93/11737 discloses a composition for removing minerals from hair which composition comprises several agents and a chelating agent. Further disclosed is a synergistic combination of chelating agents.

The compositions of the present invention containing a combination of a chelating and a sequestering agent possess the desirable properties outlined above. More in particular it has been found that adding a sequestering agent to a chelating agent potentiates the water quality improving properties of chelating agents, in particular their water softening potential. Additionally thereto, it has been found that the topical application of the compositions of this invention shows beneficial effects on a number of skin conditions and therefore the present compositions can be used as agents to prevent adverse effects on the skin as well as to treat such skin conditions.

Summary of the Invention

Thus in one aspect the present invention concerns a cosmetic or a pharmaceutical composition comprising a cosmetically or a pharmaceutically acceptable chelating agent and a cosmetically or a pharmaceutically acceptable sequestering agent.

The said composition may further contain appropriate ingredients suited for cosmetical or pharmaceutical formulations and, if desirable, further active ingredients.

In a particular aspect the composition is for topical use.

In a further particular aspect, the present invention provides a cosmetic or pharmaceutical composition comprising iminodisuccinate or a salt thereof and polyaspartic acid or a salt thereof.

In a further aspect this invention concerns the use of a composition containing a combination of a chelating agent and a sequestering agent in aqueous cosmetic or pharmaceutical compositions for reducing water hardness. The invention further concerns the use of a cosmetic or pharmaceutical composition as defined above for making water more compatible to the skin.

The invention further provides the use of a composition containing a chelating and a sequestering agent to manufacture a cosmetic or pharmaceutical composition that has increased compatability with the skin.

In still a further aspect, the invention concerns a method of treating a subject suffering from eczema, irritation and skin dryness, said method comprising topically administering an effective amount of composition comprising a cosmetically or pharmaceutically acceptable chelating agent and a cosmetically or pharmaceutically acceptable sequestering agent.

In still a further aspect, the invention concerns a cosmetic method of treating a subject suffering from eczema, irritation and skin dryness, said method comprising topically administering an effective amount of composition comprising a cosmetically acceptable chelating agent and a cosmetically acceptable sequestering agent.

The invention also concerns a process for manufacturing a cosmetic or pharmaceutical composition comprising a cosmetically or pharmaceutically acceptable chelating agent and a cosmetically or pharmaceutically acceptable sequestering agent and optional other ingredients, characterized by mixing the said chelating agent and said sequestering agent, and said optional other ingredients.

Detailed Description of the Invention

The present invention concerns cosmetic or pharmaceutical compositions comprising a cosmetically or pharmaceutically acceptable chelating agent and a cosmetically or pharmaceutically acceptable sequestering agent.

Particular chelating agents that can be used in the cosmetic or pharmaceutical compositions of this invention comprise ethylene diamino tetraacetate salts (EDTA), in particular disodium and tetrasodium ethylene diamino tetraacetate salts, and the acid form thereof; diethylene triamino pentaacetate salts (DTPA) and the acid form thereof; propylene diaminotetraacetate salts (PDTA) and the acid form thereof; hydroxyethylethylene diaminotriacetate salts (HEDTA) and the acid form thereof; tetrahydroxypropyl ethylenediamine; pentetate salts such as pentasodium pentetate and the acid form thereof; etidronate salts such as tetrasodium etidronate, and the acid form thereof; nitrilotriacetate (NTA) salts and the acid form thereof; acrylic acid/acrylamidomethyl propane sulfonic acid copolymer polyacrylate salts, and the acid form thereof; phosphonate salts and the acid form thereof; poly- or metaphosphate salts and the acid form thereof; citrate salts and citric acid, galactaric acid and galactaric acid salts; iminodisuccinate salts and the acid form thereof; zeolithe; bentonite; laminar disilicate salts and the acid form thereof; N-acylethylenediaminotriacetate salts and the acid form thereof; phytic acid and phytic acid salts.

Preferred chelating agents comprise EDTA salts and the acid form thereof; nitrilotriacetate salts and the acid form thereof; phosphonate salts and the acid form thereof; poly- or metaphosphate salts and the acid form thereof; citrate salts and citric acid; iminodisuccinate salts and the acid form thereof; bentonite; N-acylethylenediaminotriacetate salts and the acid form thereof; galactaric acid and galactaric acid salts; acrylic acid/acrylamidomethyl propane sulfonic acid copolymer salts and the acid form thereof; phytic acid and phytic acid salts.

More preferred are EDTA salts, in particular the di- and tetra- sodium or potassium EDTA salts and the acid form thereof; nitrilotriacetate salts and the acid form thereof; polycarboxylate salts and the acid form thereof; phosphonate salts and the acid form thereof; citrate salts and citric acid; phytic acid and phytic acid salts; galactaric acid or galactaric acid salts; acrylic acid/acrylamidomethyl propane sulfonic acid copolymer salts and the acid form thereof; bentonite; or iminodisuccinate salts and the acid form thereof, the latter being particularly preferred.

Particular sequestering agents that can be used in said cosmetic or pharmaceutical compositions are polyaspartic acid and its salts, cellulose derivatives, such as for example carboxymethylcellulose and salts thereof; copolymers that contain, for example, maleic or hydroxysuccinic acid as monomeric building blocks and salts thereof.

Preferred sequestering agents are polyaspartic acid and its cosmetically or pharmaceutically acceptable salts: cellulose derivatives, such as for example carboxymethylcellulose and salts thereof; copolymers that contain, for example, maleic or hydroxysuccinic acid as monomeric building blocks and salts thereof.

More preferred are cellulose derivatives, such as for example carboxymethylcellulose; and polyaspartic acid and its salts, the latter being particularly preferred.

A particular embodiment of the present invention are compositions containing a combination of iminodisuccinate salt or the acid form thereof, and polyaspartic acid or a salt thereof.

Particular salts are those which are pharmaceutically acceptable.

The compositions according to the present invention may contain one or more chelating agents and one or more sequestering agents. The term 'chelating agent' as used herein is meant to refer to one or a pluarlity of sequestering agents and similarly the term 'sequestering agent' is menat to refer to one or a plurality of sequestering agents.

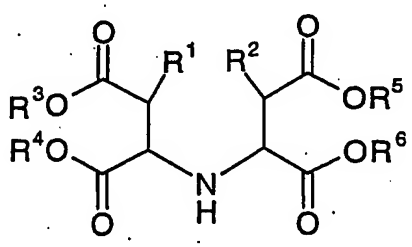
The terms 'salts' as used herein refer to cosmetically acceptable or to pharmaceutically acceptable base-addition salt forms of the components mentioned above. Cosmetically acceptable salts are those which are acceptable for topical applications and pharmaceutically acceptable salts are those which are acceptable for

topical pharmaceutical use, said salts preferably being non-toxic. Said base-addition salt forms in particular are alkali metal, e.g. sodium or potassium, or ammonium, or substituted ammonium salt forms or benzathine, *N*-methyl-D-glucamine, hydrabamine salts, or salts with amino acids such as, for example, arginine, lysine and the like. Substituted ammonium as used herein refers to any non-toxic substituted ammonium ion known or used in the art as a salt former and comprises mono-. di-, and in particular tri- or quaternary substituted ammonium salts, including mono- or polycyclic systems. Substituents on ammonium for example are alkyl, cycloalkyl, alkenyl, substituted alkyl such as hydroxyalkyl, alkyloxyalkyl, (cycloalkyl)alkyl, arylalkyl such as benzyl, and the like.

As used herein 'alkyl' refers to a saturated hydrocarbon in particular a hydrocarbon radical having one to about 20 carbon atoms, in particular 1 to about 8 carbon atoms, straight or branch chained. 'Alkyl' in hydroxyalkyl or alkoxylalkyl preferably has 2 to 6, more preferably 2 to 4 carbon atoms. 'Alkenyl' similarly refers to a hydrocarbon having one or more double bonds, e.g. one, two or three double bonds.An alkenyl radical may be staright or branch chained and may have 2 to about 20, in particular 3 to about 8 carbon atoms. Cycloalkyl may have further alkyl substituents, in particular alkyl having 1 to 6 carbon atoms, and has from 5 to 8 ring atoms.

One or more of the above base-originating kations may be present, either the same or different.

As used herein, the term 'iminodisuccinate' may refer to compounds which can be structurally represented by the following formula:



(I)

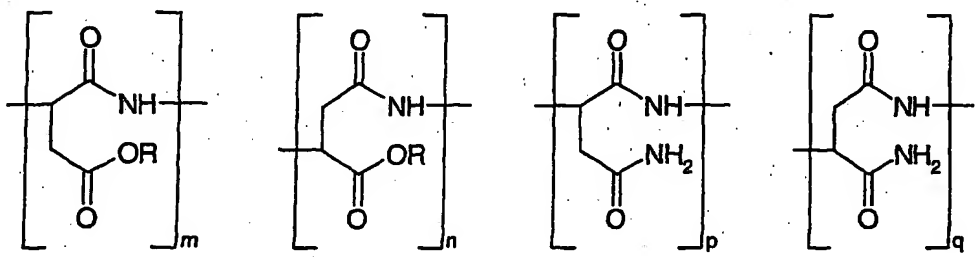
wherein:

R^1 and R^2 independently from one another represent hydrogen or hydroxy;

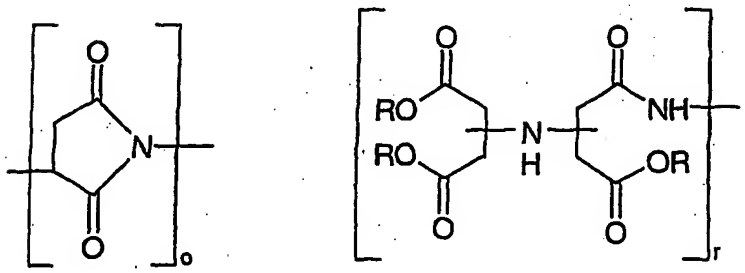
R^3, R^4, R^5 and R^6 independently from one another represent hydrogen or a suitable kation such as for example the alkali metal or ammonium kations mentioned hereinabove in relation to the term 'salts'.

In a particular embodiment the term 'imidosuccinate' as used herein refers to the compound N-(1,2-dicarboxyethyl)-aspartic acid and its salt forms. Salt forms of said compound are meant to comprise salts wherein one, two, three or four of the carboxyl hydrogens have been replaced by a suitable kation, or mixtures thereof. Examples are mono-, di-, tri- or tetra- sodium or potassium, or ammonium N-(1,2-dicarboxyethyl)-aspartic acid salts, wherein ammonium is as defined hereinabove.

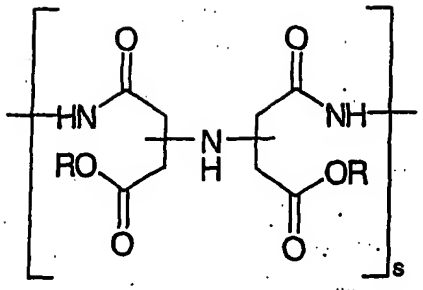
The term 'polyaspartic acid' refers to polymers made of aspartic acid monomeric units. In particular polysapartic acid comprises polymers built up of one or more different aspartic acid units being represented by the following structural formulae:



(II-a) (II-b) (II-c) (II-d)



(II-e) (II-f)



(II-g)

wherein:

each R independently represents hydrogen or a suitable kation such as for example the alkali metal or ammonium kations mentioned hereinabove in relation to the term 'salts';

m, n, o, p, q, r and s independently from one another are 0 or an integer up to 300, preferably up to 100, more preferably up to 50, whereby the sum of m + n + o + p + q + r + s is in the range of 4 to 300, preferably 4 to 100, more preferably 4 to 50, still more preferably between 10 to 40, most preferably between 15 and 30.

Preferred polymers are those wherein:

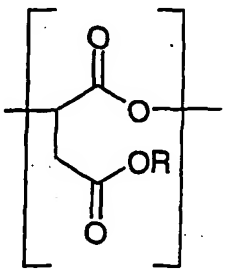
p and q independently are 0 or an integer from 1 to 10;

r is 0 or the integer 1 or 2;

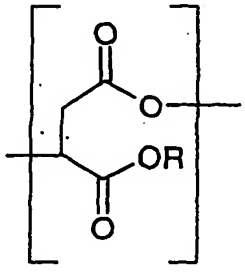
s is 0 or an integer from 1 to 10.

Other polyaspartic acids that can be used are those, as defined hereinabove, wherein part of the above referred monomeric units is replaced by analogs such as:

malic acid units of formula



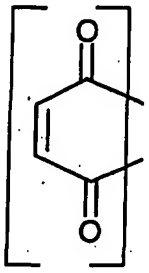
(II-h)



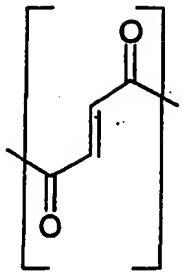
(II-i)

wherein R is as defined above;

maleic acid and and fumaric acid units of formula



(II-j)

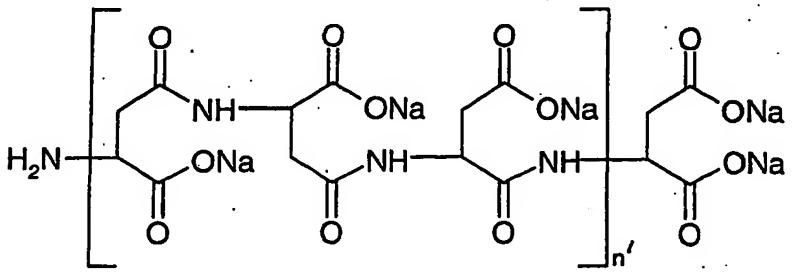


(II-k)

In particular up to 10 monomeric units per polymeric molecule, more particularly up to 5 units, e.g. 1 or 2 units, may be replaced by any of the above malic, maleic or fumaric residues.

Preferably, the polyaspartic acid used in the formulations of the invention has a mean molar mass in the range of about 500 to about 100,000 g/mole, in particular in the range of 1000 to 50,000 g/mole, more in particular between 1000 and 30,000. Preferred is a mean molar mass in the range of 800 to 5000 g/mol, more preferably in the range of about 1000 to 4000 g/mol, still more preferably in the range of about 1500-3000 g/mol.

A particularly preferred polyaspartic acid or a salt thereof can be represented by the following structural formula:



(III)

wherein n' is an integer in the range of 1 to 300, preferably 1 to 100, more preferably 1 to 50, or 1 to 40, or 4 to 30, most preferably between 15 and 30.

In the compounds of formula (III) some or all of the sodium kations may be replaced by one or more kations selected from hydrogen or the other alkalimetal kations, in particular potassium or ammonium or substituted ammonium.

Also particularly preferred are the potassium analogs of said particularly polyaspartic acid salt, or the acid itself. Of further interest is the above particularly preferred polyaspartic sodium or potassium salt wherein one or more of the sodium or potassium kations are replaced by hydrogen ions, more in particular wherein one or two sodium or potassium kations per monomeric unit are replaced by hydrogen ions.

The concentration of the chelating and sequestering agent in the compositions of the invention may vary but will in general be such that a sufficient reduction of the concentration of free calcium and/or magnesium ions and/or other metal ions causing problems like iron, copper, manganese etc. is obtained. In particular the concentration of the chelating agent will be from 0,1 – 95 %, preferably from 0,2 – 90 %, more preferably from 0,4 – 85 % w/w relative to the total weight of the composition. In particular the concentration of the sequestering agent will be from 0 – 45 %, or from 0.1 – 45 %, preferably from 0,1 – 40 %, more preferably from 0,2 – 35 % w/w relative to the total weight of the composition.

The w/w ratio of the chelating and sequestering agent preferably is in the range of from 20 : 1 to 1 : 20, more preferably from 10 : 1 to 1 : 10 most preferably from 5 : 1 to 1 : 5.

In the compositions of the invention, the w/w ratio of the chelating and sequestering agents may vary as described above, but also formulations having a low content of sequestering agent, i.e. where the w/w ratio of the chelating agent to the sequestering agent is 10 : 1 or higher, or 20 : 1 or higher, e.g. in the range of 20 : 1 to 25 : 1, or 25 : 1 to 30 : 1, or even 30 : 1 to 40 : 1 or to 50 : 1 are desirable combinations forming compositions with the attractive properties described herein. Even the extreme case where no sequestering agent is present gives rise to formulations having beneficial properties described herein, which is an additional feature of this invention.

In the particular compositions containing a combination of iminodisuccinate salt or the acid form thereof, and polyaspartic acid or a salt thereof the w/w ratio may vary as described above. Also in this instance, even the extreme case where no polyaspartic acid is present gives rise to formulations having the beneficial properties described herein.

The cosmetic and pharmaceutical compositions according to the present invention may additionally contain further ingredients or additives such as surfactants, emulsifiers, consistency factors, conditioners, emollients, skin caring ingredients, moisturizers, thickeners, tablet disintegrants, glidants, lubricants, fillers, binding agents, anti-oxidants, preservatives, active ingredient, in particular dermatologically active ingredients, fragrances and the like. Active ingredients as mentioned herein comprise, for example, anti-inflammatories, anti-bacterials, anti-fungals and the like agents. Active ingredients suited for topical applications are particularly preferred.

Suitable surfactants comprise:

alkyl sulfates e.g. sodium lauryl sulfate, ammonium lauryl sulfate, sodium cetearyl sulfate,

alkyl sulfoacetates e.g. sodium lauryl sulfoacetate,

alkyl ether sulfates e.g. sodium laureth sulfate, sodium trideceth sulfate, sodium oleth sulfate, ammonium laureth sulfate,

alkyl ether sulfosuccinates e.g. disodium laureth sulfosuccinate,

alkyl glycosides e.g. decyl glucoside, lauryl glucoside,

alkyl isethionates,

amphoterics e.g. cocamidopropyl betaine, sodium cocoamphoacetate, sodium lauroamphoacetate, disodium lauroamphodiacetate, disodium cocoamphodiacetate, sodium lauroamphopropionate, disodium lauroamphodipropionate, potassium or ammonium slats of the aforementioned amphoterics, capryl/capramidopropyl betaine, undecylenamidopropyl betaine, lauramidopropyl betaine and

fatty alcohol polyglycol ethers.

Suitable emulsifiers are e.g. anionics as salts of fatty acids e.g. sodium stearate or sodium palmitate, organic soaps e.g. mono-, di- or triethanolaminoleat, sulfated or sulfonated compounds e.g. sodium lauryl sulfate or sodium cetyl sulfonate, saponines, lamepones; cationics as quaternary ammonium salts; nonionics as fatty alcohols, fatty acid ester with saturated or unsaturated fatty acids, polyoxyethylenesters or polyoxyethylenethers of fatty acids, polymers from ethylene oxide and propylene oxide or propylene glycol, amphotherics as phosphatides, proteines as gelatine, casein alkylamidobetaines, alkyl betaines and amphoglycinates, alkyl phosphates, alkylpolyoxyethylene phoaphates or the corresponding acids, silicone derivatives, e.g. alkyl dimethiconecoplyol.

Suitable consistency factors are e.g. fatty alcohols or their mixtures with fatty acid esters, e.g. acetylated lanolin alcohol, aluminum stearates, carbomer, cetyl alcohol, glyceryl oleate, glyceryl stearate, glyceryl stearate (and) PEG 100 stearate, magnesium stearate, magnesium sulfate, oleic acid, stearic acid, stearyl alcohol, myristyl myristate, isopropyl palmitate, beeswax and synthetic equivalents thereof, carbomers, etc. Suitable conditioners are e.g. alkylamido ammonium lactate, cetrimonium chloride and distearoylethyl hydroxyethylmonium methosulfate and cetearyl alcohol, cetyl dimethicone, cetyl ricinoleate, dimethicone, laureth-23, laureth-4, polydecene, retinyl palmitate, quaternised protein hydrolysates, quaternised cellulose and starch derivatives, quaternised copolymers of acrylic or methacrylic acid or salts, quaternised silicone derivatives.

Suitable emollients are e.g. cetearyl isononanoate, cetearyl octanoate, decyl oleate, isooctyl stearate, coco caprylate/caprate, ethylhexyl hydroxystearate, ethylhexyl isononanoate, isopropyl isostearate, isopropyl myristate, oleyl oleate, hexyl laurate, paraffinum liquidum, PEG-75 lanolin, PEG-7 glyceryl cocoate, petrolatum, ozokerite, cyclomethicone, dimethicone, dimethicone copolyol, dicaprylyl ether, Butyrospermum parkii, Buxus chinensis, canola, Carnauba cera, copernicia cerifera, Oenothera biennis, Elaeis guineensis, Prunus dulcis, squalane, Zea mays, glycine soja, Helianthus annuus, lanolin, hydrogenated castor oil, hydrogenated coconut oil, hydrogenated polyisobutene, sucrose cocoate, stearoxy dimethicone, lanolin alcohol, isohexadecane.

Suitable skin caring ingredients are e.g. plant extracts, bisabolol, antiinflammatory agents, urea, allantoin, panthenol and panthenol derivatives, phytantriol, vitamines A, E, C, D, ceramides of animal or plant origin, lecithins, and the like.

Suitable moisturizers are e.g. butylene glycol, cetyl alcohol, dimethicone, dimyristyl tartrate, glucose, glycereth-26, glycerin, glyceryl stearate, hydrolyzed milk protein, lactic acid, lactose and other sugars, laureth-8, lecithin, octoxyglycerin, PEG-12, PEG-135, PEG-150, PEG-20, PEG-8, pentylene glycol, hexylene glycol, phytantriol, polyquaternium-39, PPG-20 methyl glucose ether, propylene glycol, sodium hyaluronate, sodium lactate, sodium PCA, sorbitol, succinoglycan, synthetic beeswax, tri-C14-15 alkyl citrate, starch, and the like.

Suitable thickeners are e.g. acrylates/steareth-20 methacrylate copolymer, carbomer, carboxymethyl starch, cera alba, dimethicone/vinyl dimethicone

crosspolymer, propylene glycol alginate, hydroxyethylcellulose, hydroxypropyl methylcellulose, silica, silica dimethyl silylate, xanthan gum, hydrogenated butylene/ethylene/styrene copolymer, and the like.

Suitable tablet disintegrants are e.g. starch, sodium starch glycolate, crospovidone, sodium croscarmellose, alginic acid and alginates, calcium carbonate, sodium bicarbonate, magnesium peroxide, amylose, sodium and calcium carboxymethylcellulose, polyvinylpyrrolidone, cetyl alcohol, glycerin monostearate, lactose, and the like.

Suitable fillers are e.g. tricalciumphosphate, starch, sugar, lactic sugar, glucose, sodium chloride, and the like.

Suitable glidants are e.g. starch, magnesium stearate, calcium stearate, silica (Aerosil®/Cabosil®), amylose, talcum, tricalciumphosphate, magnesium oxide, calcium and magnesium carbonate, trimagnesium phosphate, tetrasodium diphosphate, silicium dioxide, aluminium silicate, kaolin, calcium and magnesium silicate, bentonite, magnesium trisilicate, calcium gluconate, salts of myristic, palmitic or stearic acid, sodium aluminium silicate.

Suitable lubricants are e.g. adipic acid, fumaric acid and its salts, benzoic acid and its salts, glycerine triacetate, sodium or magnesium lauryl sulfate, magnesium stearate, solid polyethylenglycol, polyvinylpyrrolidone, boric acid, monolaurate or – palmitate, myristyl alcohol, cetyl alcohol, cetylstearyl alcohol, talcum, calcium or magnesium salts of higher fatty acids, mono-, di- or triglycerides of higher fatty acids, polytetrafluorethylene.

Suitable binding agents are e.g. starch, carboxymethylcellulose, polyvinylpyrrolidone, gummi arabicum, calcium sulphate, calcium phosphate, veegum, sorbitol, sodium alginate, gelatine and the like.

Suitable anti-oxidants are e.g. sulfites, e.g. sodium sulfite, tocopherol or derivates thereof, ascorbic acid or derivates thereof, citric acid, propyl gallate, chitosan glycolate, cysteine, N-acetyl cysteine plus zinc sulfate, thiosulfates, e.g. sodium thiosulfate, polyphenoles and the like.

Suitable preservatives are e.g. benzyl alcohol, chloroxylenol, (sodium) methylparaben, (sodium) ethylparaben, (sodium) propylparaben, (sodium) butylparaben, phenoxyethanol, methylchloroisothiazolinone, methylisothiazolinone, sodium benzoate, chlorhexidine digluconate methyldibromoglutaronitrile, sodium borate, 5-bromo-5-nitro-1,3-dioxane, alcohol, benzoic acid, dehydroacetic acid, diazolidinyl urea, dichlorobenzyl alcohol, glucose oxidase, hexamidine diisethionate, imidazolidinyl urea, iodopropynyl butylcarbamate, isobutylparaben, isopropylparaben, lactoperoxidase, magnesium nitrate, PEG-4 laurate, phenethyl alcohol, polyaminopropyl biguanide, potassium sorbate, propylene glycol, pyridoxine HCl, quaternium-15, sorbic acid, triclosan and mixtures thereof.

The compositions may further contain active ingredients, e.g. anti-microbials such as complexes of PVP and hydrogen peroxide, anti-inflammatories as, plant extracts, bisabolol, panthenol, tocopherol, actives for anti-stinging, anti-irritants, anti-dandruffs, for anti-ageing e.g. retinol, melibiose etc. Other suitable actives are e.g. Medicago officinalis, Actinidia chinensis, allantoin, Aloe barbadensis, Anona cherimolia, Anthemis nobilis, Arachis hypogaea, Arnica montana, Avena sativa, beta-carotene, bisabolol, Borago officinalis, butylene glycol, Calendula officinalis, Camellia sinensis, camphor, Candida bombicola, capryloyl glycine, Carica papaya, Centaurea cyanus, cetylpyridinium chloride, Chamomilla recutita, Chenopodium quinoa, Chinchona succirubra, Chondrus crispus, Citrus aurantium dulcis, Citrus grandis, Citrus limonum, Cocos nucifera, Coffea arabica, Crataegus monogina, Cucumis melo, dichlorophenyl imidazoldioxolan, Enteromorpha compressa, Equisetum arvense, ethoxydiglycol, ethyl panthenol, farnesol, ferulic acid, Fragaria chiloensis, Gentiana lutea, Ginkgo biloba, glycerin, glyceryl laurate, Glycyrrhiza glabra, Hamamelis virginiana, heliotropine, hydrogenated palm glycerides, citrates, hydrolyzed castor oil, hydrolyzed wheat protein, Hypericum perforatum, Iris florentina, Juniperus communis, lactis proteinum, lactose, Lawsonia inermis, linalool, Linum usitatissimum, lysine, Magnesium aspartate, magnifera indica, Malva sylvestris, mannitol, mel, Melaleuca alternifolia, Mentha piperita, menthol, menthyl lactate, Mimosa tenuiflora, Nymphaea alba, olaflur, Oryza sativa, panthenol, paraffinum liquidum, PEG-20M, PEG-26 jojoba acid, PEG-26 jojoba alcohol, PEG-35 castor oil, PEG-40 hydrogenated castor oil, PEG-60 hydrogenated castor oil, PEG-8 caprylic/capric acid, Persea gratissima, petrolatum, potassium aspartate, potassium sorbate, propylene glycol, Prunus amygdalus dulcis, prunus armeniaca, Prunus persica, retinyl palmitate, Ricinus communis, Rosa canina, Rosmarinus officinalis, rubus idaeus, salicylic acid, Sambucus nigra, sarcosine, Serenoa serrulata, Simmondsia chinensis, sodium carboxymethyl betaglucan, sodium

cocoyl amino acids, sodium hyaluronate, sodium palmitoyl proline, stearoxytrimethylsilane, stearyl alcohol, sulfurized TEA-ricinoleate, talcum, thymus vulgaris, Tilia cordata, tocopherol, tocopheryl acetate, trideceth-9, Triticum vulgare, tyrosine, undecylenoyl glycine, urea, Vaccinium myrtillus, valine, zinc oxide, zinc sulfate and the like

The compositions of the present invention are generally prepared by mixing the appropriate chelating and sequestering agents and other ingredients. Subsequently other ingredients, such as perfumes, may be added.

A number of the properties of the present compositions and and the results of their use in the methods of the present invention, as described herein, are due to the combination of a chelating and a sequestering agent, and are either more beneficial than in compositions with only one of said agents.

The compositions of the present invention comprising imidodisuccinate or salts thereof, and polyaspartic acid and salts thereof, as defined or described herein, are particular attractive due to their increased biodegredability which makes them environmentally more acceptable.

The compositions of the invention may take the form of a stand alone product, i.e. an additive to baths, shampoos and the like, or a combination product. They may be solid, semi-solid or liquid, for example they can be solutions, emulsions, pastes, powders, granulates, tablets, effervescent tablets, gels, wet or dry wipes and the like.

The cosmetic or pharmaceutical preparations of the invention can be used to improve water quality, either in other aqueous formulations, both pharmaceutical and cosmetical, in particular for topical application, or in aquous media for sanitary applications such as bathing water.

Therefore in a further aspect the invention provides a method of improving water quality in topical pharmaceutical compositions or in cosmetical compositions aqueous media for sanitary applications, said method comprising adding to said pharmaceutical or said cosmetic or said aqueous media a composition comprising a cosmetically or pharmaceutically acceptable chelating agent and a cosmetically or pharmaceutically acceptable sequestering agent.

Or simularly, the invention provides the use of a composition according to the present invention to improve water quality in topical pharmaceutical compositions or in cosmetical compositions aqueous media for sanitary applications.

As used herein water quality refers to water hardness, smell, appearance (colour), and the presence of solids, the latter including the presence solids upon contact with soap, detergents, shampoo and the like.

In view of these properties compositions like e.g. bath or shower gels, are particularly attractive. Of particular interest are compositions for use with babies, infants or small children.

The compositions of the present invention show activity against a number of skin conditions such as eczema, irritation and skin dryness or prevent them when used in conjunction with cleansing before these conditions arise. These skin conditions may be treated by topically administering an appropriate composition according to this inventions such as an ointment, salve, lotion and the like. Or alternatively the compositions may be added to water in which the affected is immerged or as a bathing or showering additive. They especially render the water used for cleansing more compatible to skin.

In the light of this activity, the invention further is concerned with a method of treating subjects suffering from skin conditions such as eczema, irritation and skin dryness, said method comprising the topical administration of a composition comprising an effective amount of a chelating and sequestering agent. Or there is provided the use of a combination of a chelating and a sequestring agent, or a pharmaceutical composition comprising a chelating and a sequestering agent for the manufacture of a medicament for topically treating a skin condition such as eczema, irritation and skin dryness.

The following examples are meant to illustrate the invention, not to limit it thereto. As used herein, percentages of chelating or sequestering agents are w/w percentages of the solid material in water.

Examples

Example 1: Powder

Ingredient	weight [%]
Sodium bicarbonate	41.67
Citric acid	52.38
Sodium polyaspartic acid (82 %)	1.19
Imino disuccinate (76 %)	3.57
Tapioca starch	0.60
Perfume	0.60

Blend all ingredients under dry conditions.

Example 2: Powder

Sodium bicarbonate	41.67
Citric acid	52.38
Sodium polyaspartic acid (82 %)	1.19
Nitrilotriacetic trisodium salt	3.57
Tapioca starch	0.60
Perfume	0.60

Blend all ingredients under dry conditions.

Example 3: Powder with surfactant

Sodium bicarbonate	37.23
Citric acid	46.81
Sodium lauryl sulfoacetate	10.64
Sodium polyaspartic acid (82 %)	1.06
Imino disuccinate (76 %)	3.19
Tapioca starch	0.53
Perfume	0.53

Blend all ingredients under dry conditions.

Example 4: Powder with surfactant

Sodium bicarbonate	37.23
Citric acid	46.81
Sodium lauryl sulfoacetate	10.64
Sodium polyaspartic acid (82 %)	1.06
EDTA (trisodium salt)	3.19
Tapioca starch	0.53
Perfume	0.53

Blend all ingredients under dry conditions.

Example 5: Liquid

Sodium polyaspartic acid (40 %)	0.50
Imino disuccinate (34 %)	6.00
Extrapone Camomile special®	1.00
Sodium sulphite	0.50
Phenoxyethanol	1.00
Aqua	87.70
Perfume	0.30
Polysorbate	2.00
Lactic acid	1.00

Mix ingredients stirring into water. Add perfume premixed with polysorbate. Adjust pH to 6-7.

Example 6: Liquid

Sodium polyaspartic acid (40 %)	0.50
HEDTA (trisodum salt)	6.00
Extrapone Camomile special®	1.00
Sodium sulphite	0.50
Phenoxyethanol	1.00
Aqua	87.70
Perfume	0.30

Polysorbate	2.00
Lactic acid	1.00

Mix ingredients stirring into water. Add perfume premixed with polysorbate. Adjust pH to 6-7.

Example 7: Liquid with anti-microbial

Sodium polyaspartic acid (40%)	3.50
Imino disuccinate (34%)	7.00
Extrapone Camomile special®	3.00
Polyquaternium-47	1.00
PVP-H_2O_2	1.00
Phenoxyethanol	0.80
Aqua	77.85
Lactic acid	1.00
Polysorbate	4.00
Perfume	0.35
Dye (0,1 %)	0.50

Stir ingredients into water phase. Add perfume premixed with polysorbate. Adjust pH to 6-7.

Example 8: Liquid with anti-microbial

Carboxymethylcellulose	3.50
DTPA (trisodium salt)	7.00
Extrapone Camomile special®	3.00
Polyquaternium-47	1.00
PVP-H_2O_2	1.00
Phenoxyethanol	0.80
Aqua	77.85
Lactic acid	1.00
Polysorbate	4.00
Perfume	0.35
Dye (0,1 %)	0.50

Stir ingredients into water phase. Add perfume premixed with polysorbate. Adjust pH to 6-7.

Example 9: Liquid as bath product

Sodium polyaspartic acid (40%)	5.00
Imino disuccinate (34%)	5.00
Sodium laureth sulphate	4.30
Decyl glucoside	4.00
Cocamidopropyl betaine	7.90
Lauryl betaine	2.30
Phenoxyethanol	0.80
Sodium propylparaben	0.11
Sodium methylparaben	0.17
Sodium butylparaben	0.06
Aqua	69.86
Perfume	0.50

Stir ingredients into water phase. Add perfume premixed with polysorbate. Adjust pH to 6-7.

Example 10: Tablets

Sodium bicarbonate	40.00
Citric acid	32.00
Magnesium stearate	1.00
Sodium polyaspartic acid (82 %)	5.00
Polyethylenglycol	5.00
Imino disuccinate (76 %)	13.00
Sodium carboxymethyl cellulose	3.00
Silica	1.00

Mix all ingredients thoroughly and press the mixture to tablets.

Example 11: Tablets

Sodium bicarbonate	40.00
Citric acid	32.00
Magnesium stearate	1.00
Sodium polyaspartic acid (82 %)	5.00
Polyethylenglycol	5.00
EDTA (trisodium salt)	13.00
Sodium carboxymethyl cellulose	3.00
Silica	1.00

Mix all ingredients thoroughly and press the mixture to tablets.

Example 12: Tablets with surfactant

Sodium bicarbonate	37.23
Citric acid	46.81
Sodium lauryl sulfoacetate	10.64
Sodium polyaspartic acid (82 %)	1.06
Imino disuccinate (76 %)	3.19
Tapioca starch	0.53
Perfume	0.53

Mix all ingredients thoroughly with the premix perfume and topioca starch. Then compress the mixture to tablets.

Example 13: Tablets with surfactant

Sodium bicarbonate	37.23
Citric acid	46.81
Sodium lauryl sulfoacetate	10.64
Sodium polyaspartic acid (82 %)	1.06
NTA (trisodium salt)	3.19
Tapioca starch	0.53
Perfume	0.53

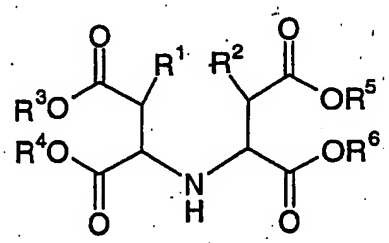
Mix all ingredients thoroughly with the premix perfume and topioca starch. Then compress the mixture to tablets..

We claim:

1. A cosmetic or pharmaceutical composition comprising a cosmetically or a pharmaceutically acceptable chelating agent and a cosmetically or a pharmaceutically acceptable sequestering agent.

2. A composition according to claim 1, wherein the chelating agent is selected from the group consisting of iminodisuccinate salts and the acid form thereof; and wherein the sequestering agent is selected from the group consisting of polyaspartic acid and its salts.

3. A composition according to claim 2 wherein the chelating agent is a compound which can be structurally represented by the formula:



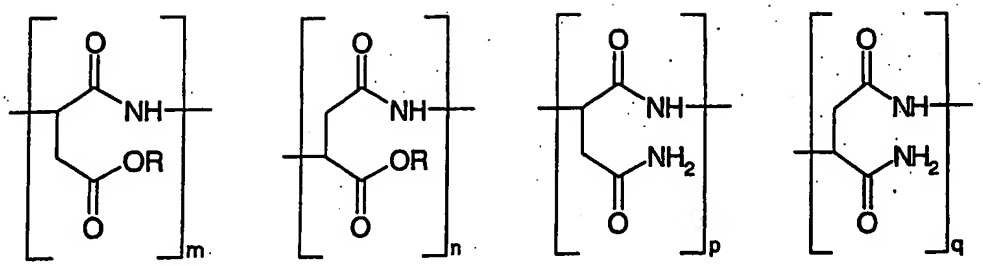
(I)

wherein:

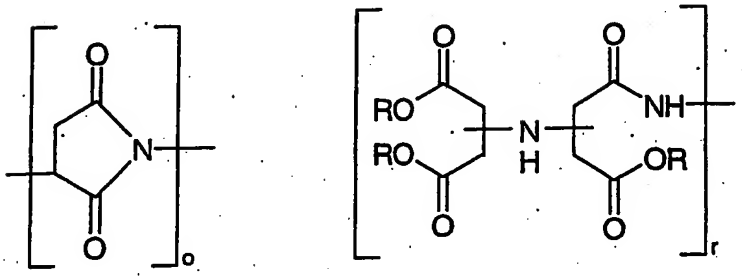
R^1 and R^2 independently from one another represent hydrogen or hydroxy;

R^3, R^4, R^5 and R^6 independently from one another represent hydrogen or an alkali metal or ammonium or substituted ammonium kation;

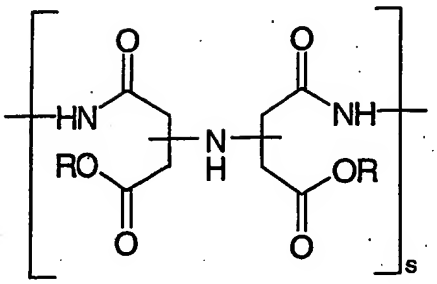
and the sequestering agent is a polymer built up of one or more aspartic acid units which can be represented by the following structural formulae:



(II-a) (II-b) (II-c) II-d)



(II-e) (II-f)



(II-g)

wherein:

each R independently represents hydrogen or a suitable kation;

m, n, o, p, q, r and s independently from one another are 0 or an integer up to 300, whereby the sum of m + n +o + p +q + r + s is in the range of 4 to 300.

4. A composition according to claim 3 wherein the chelating agent is a polyaspartic acid as defined in claim 3 wherein

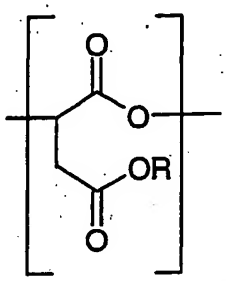
p and q independently are 0 or an integer from 1 to 10;

r is 0 or the integer 1 or 2;

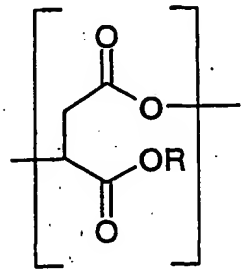
s is 0 or an integer from 1 to 10.

5. A composition according to any of claims 3 or 4 wherein the chelating agent is a polyaspartic acid as defined in claims 3 or 4, wherein part of the monomeric units is replaced by analogs such as:

malic acid units of formula



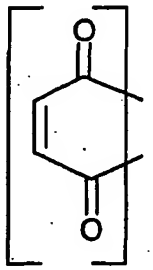
(II-h)



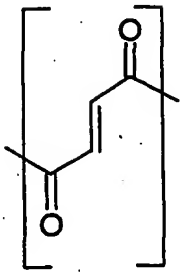
(II-i)

wherein R is as defined above;

maleic acid and and fumaric acid units of formula



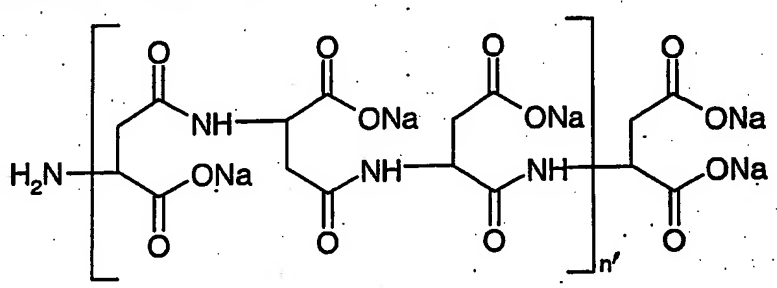
(II-j)



(II-k)

6. A composition according to claim 5 wherein up to 10 monomeric units per polymeric molecule may be replaced by any of the malic, maleic or fumaric residues defined in claim 5.

7. A composition according to any of claims 2 to 4 wherein the polyaspartic acid or its salt-form can be represented by the following formula:



(III)

wherein n' is an integer in the range of 1 to 300;

and wherein some or all of the sodium kations may be replaced by one or more kations selected from hydrogen, potassium, ammonium or substituted ammonium.

8. A composition according to any of claims 1-2, wherein the chelating agent is N- (1, 2 - dicarboxyethyl) - aspartic acid or a salt thereof; and the sequestering agent is a polyaspartic acid salt represented by the structural formula (III) as defined in claim 7.

9. A composition according to claim 1, wherein the chelating agent is selected from the group consisting of ethylene diamino tetraacetate salts (EDTA), and the acid form thereof; diethylene triamino pentaacetate salts (DTPA) and the acid form thereof; propylene diaminotetraacetate salts (PDTA) and the acid form thereof; hydroxyethylethylene diaminotriacetate salts (HEDTA) and the acid form thereof; tetrahydroxypropyl ethylenediamine; pentetate salts and the acid form thereof; etidronate salts, and the acid form thereof; nitrilotriacetate (NTA) salts and the acid form thereof; acrylic acid/acrylamidomethyl propane sulfonic acid copolymer polyacrylate salts, and the acid form thereof; phosphonate salts and the acid form thereof; poly- or metaphosphate salts and the acid form thereof; citrate salts and citric acid; galactaric acid and galactaric acid salts; iminodisuccinate salts and the acid form thereof; zeolithe; bentonite; laminar disilicate salts and the acid form thereof; N-

acylethylenediaminotriacetate salts and the acid form thereof; phytic acid and phytic acid salts;

and wherein the sequestering agent is selected from the group consisting of polyaspartic acid and its salts; cellulose derivatives; copolymers that contain, maleic or hydroxysuccinic acid as monomeric building blocks and salts thereof.

10. A composition according to claims 1-9, wherein the chelating agent is present in a concentration in the range of 0,1 - 95 % and the sequestering agent is present in a concentration in the range of 0 – 45 %, w/w relative to the total weight of the composition.

11. A composition according to claims 1-9, wherein the chelating agent is present in a concentration in the range of 0,4 - 85 % and the sequestering agent in a concentration in the range of 0,2 - 35 %, w/w relative to the total weight of the composition.

12. A composition according to claims 1-9, wherein the weight ratio of the chelating agent to the sequestering agent is in the range between 20 :1 and 1 : 20, in particular in the range between 10 :1 and 1 : 10, more in particular in the range between 5 :1 and 1 : 5.

13. A composition according to claims 1-12 further containing an antibacterial, an antiinflammatory or a plant extract.

14. Use of a combination of pharmaceutically acceptable chelating agent and a pharmaceutically acceptable sequestering agent as a medicine.

15. Use of a pharmaceutical composition as claimed in any of claims 1-13 as a medicine for the manufacture of a medicament for the topical treatment of eczema, irritation or skin dryness.

(12) NACH DEM VERTRAG ÜBER DIE INTERNATIONALE ZUSAMMENARBEIT AUF DEM GEBIET DES PATENTWESENS (PCT) VERÖFFENTLICHTE INTERNATIONALE ANMELDUNG

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(84) Bestimmungsstaaten *(regional)*: europäisches Patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR).

Erklärung gemäß Regel 4.17:
— *Erfindererklärung (Regel 4.17 Ziffer iv) nur für US*

Veröffentlicht:
— *mit internationalem Recherchenbericht*

(88) Veröffentlichungsdatum des internationalen Recherchenberichts: 25. September 2003

Zur Erklärung der Zweibuchstaben-Codes und der anderen Abkürzungen wird auf die Erklärungen ("Guidance Notes on Codes and Abbreviations") am Anfang jeder regulären Ausgabe der PCT-Gazette verwiesen.

WO 03/020239 A3

(54) Title: INCREASE IN THE SKIN-MOISTURISING PROPERTIES OF POLYOLS

(54) Bezeichnung: ERHÖHUNG DER HAUTBEFEUCHTENDEN EIGENSCHAFTEN VON POLYOLEN

(57) Abstract: Cosmetic and/or dermatological preparations comprising a) iminodisuccinic acid and/or salts thereof b) polyols along with other active ingredients, adjuncts and additives.

(57) Zusammenfassung: Kosmetische und/oder dermatologische Zuberreitungen enthaltend a) Iminodibernsteinsäure und/oder ihre Salze b) Polyole neben anderen Wirk-, Hilfs- und Zusatzstoffen.

INTERNATIONALER RECHERCHENBERICHT

Internes Aktenzeichen
PCT/EP 02/09577

A. KLASSIFIZIERUNG DES ANMELDUNGSGEGENSTANDES
IPK 7 A61K7/48 A61P17/00 A61K31/19

Nach der Internationalen Patentklassifikation (IPK) oder nach der nationalen Klassifikation und der IPK

B. RECHERCHIERTE GEBIETE

Recherchierter Mindestprüfstoff (Klassifikationssystem und Klassifikationssymbole)
IPK 7 A61K

Recherchierte aber nicht zum Mindestprüfstoff gehörende Veröffentlichungen, soweit diese unter die recherchierten Gebiete fallen

Während der internationalen Recherche konsultierte elektronische Datenbank (Name der Datenbank und evtl. verwendete Suchbegriffe)
EPO-Internal, WPI Data, PAJ, CHEM ABS Data

C. ALS WESENTLICH ANGESEHENE UNTERLAGEN

Kategorie*	Bezeichnung der Veröffentlichung, soweit erforderlich unter Angabe der in Betracht kommenden Teile	Betr. Anspruch Nr.
P,X	WO 02 19981 A (JOHNSON & JOHNSON) 14. März 2002 (2002-03-14) Seite 12, Zeile 28 - Zeile 34; Ansprüche 1-3,9-11,15; Beispiel 7	1-9
P,X	DE 100 34 101 A (BEIERSDORF) 24. Januar 2002 (2002-01-24) Seite 5, Zeile 10 - Zeile 15; Ansprüche 1,2,4; Beispiel 9	1-9
P,X	DE 100 34 102 A (BEIERSDORF) 24. Januar 2002 (2002-01-24) Seite 4, Zeile 56 - Zeile 62; Ansprüche 1,2,4; Beispiele 4,6	1-9

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[X] Weitere Veröffentlichungen sind der Fortsetzung von Feld C zu entnehmen

[X] Siehe Anhang Patentfamilie

* Besondere Kategorien von angegebenen Veröffentlichungen :
"A" Veröffentlichung, die den allgemeinen Stand der Technik definiert, aber nicht als besonders bedeutsam anzusehen ist
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Datum des Abschlusses der internationalen Recherche	Absendedatum des internationalen Recherchenberichts
13. März 2003	21/03/2003

Name und Postanschrift der Internationalen Recherchenbehörde	Bevollmächtigter Bediensteter
Europäisches Patentamt, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Willekens, G

INTERNATIONALER RECHERCHENBERICHT

Internationales Aktenzeichen
PCT/EP 02/09577

C.(Fortsetzung) ALS WESENTLICH ANGESEHENE UNTERLAGEN

Kategorie*	Bezeichnung der Veröffentlichung, soweit erforderlich unter Angabe der in Betracht kommenden Teile	Betr. Anspruch Nr.
P,X	DE 101 00 720 A (BEIERSDORF) 11. Juli 2002 (2002-07-11) Seite 9, Zeile 64 - Zeile 68; Ansprüche 1-3; Beispiele 3,14,16	1-9

INTERNATIONALER RECHERCHENBERICHT

Angaben zu Veröffentlichungen, die zur selben Patentfamilie gehören

Interne s Aktenzeichen
PCT/EP 02/09577

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			WO	0219981 A2	14-03-2002
DE 10034101	A	24-01-2002	DE	10034101 A1	24-01-2002
DE 10034102	A	24-01-2002	DE	10034102 A1	24-01-2002
DE 10100720	A	11-07-2002	DE	10100720 A1	11-07-2002
			WO	02055050 A1	18-07-2002

INTERNATIONAL SEARCH REPORT

Inten pplication No
PCT/EP 02/09577

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K7/48 A61P17/00 A61K31/19

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 02 19981 A (JOHNSON & JOHNSON) 14 March 2002 (2002-03-14) page 12, line 28 - line 34; claims 1-3,9-11,15; example 7 ---	1-9
P,X	DE 100 34 101 A (BEIERSDORF) 24 January 2002 (2002-01-24) page 5, line 10 - line 15; claims 1,2,4; example 9 ---	1-9
P,X	DE 100 34 102 A (BEIERSDORF) 24 January 2002 (2002-01-24) page 4, line 56 - line 62; claims 1,2,4; examples 4,6 ---	1-9

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
13 March 2003	21/03/2003

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Willekens, G

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	DE 101 00 720 A (BEIERSDORF) 11 July 2002 (2002-07-11) page 9, line 64 - line 68; claims 1-3; examples 3,14,16	1-9

INTERNATIONAL SEARCH REPORT

Information on patent family members

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